

THE CLAIMS

What is claimed is:

- 5 1. A method of treating or preventing a disorder that is ameliorated by the inhibition of neuronal monoamine reuptake which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a bupropion metabolite, or a pharmaceutically acceptable salt, solvate, or clathrate thereof.
- 10 2. The method of claim 1 wherein the bupropion metabolite is optically pure.
3. The method of claim 2 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.
- 15 4. The method of claim 1 wherein the adverse effects associated with the inhibition of dopamine reuptake are reduced or avoided.
5. The method of claim 1 wherein the bupropion metabolite or
- 20 pharmaceutically acceptable salt, solvate, or clathrate thereof is adjunctively administered with a second pharmacologically active compound.
6. A method of treating or preventing erectile dysfunction which comprises administering to a patient in need of such treatment or prevention a therapeutically or
- 25 prophylactically effective amount of a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.
7. The method of claim 6 wherein the bupropion metabolite is optically pure.
- 30 8. The method of claim 7 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.

9. The method of claim 6 wherein the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is administered transdermally or mucosally.

5 10. The method of claim 6 wherein the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is adjunctively administered with a 5-HT₃ antagonist.

10 11. The method of claim 10 wherein the 5-HT₃ antagonist is an antiemetic agent.

12. The method of claim 10 wherein the 5-HT₃ antagonist is selected from the group consisting of granisetron, metoclopramide, ondansetron, renzapride, zacopride, tropisetron, and optically pure stereoisomers, active metabolites, and pharmaceutically acceptable salts, solvates, and clathrates thereof.

15 13. A method of treating or preventing an affective disorder which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.

20 14. The method of claim 13 wherein the bupropion metabolite is optically pure.

15 15. The method of claim 14 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.

25 16. The method of claim 13 wherein the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is adjunctively administered with a therapeutically or prophylactically effective amount of a second pharmacologically active compound.

30 17. The method of claim 13 wherein the affective disorder is depression.

18. The method of claim 13 wherein the affective disorder is narcolepsy.
19. The method of claim 13 wherein the affective disorder is nicotine addiction.
- 5 20. A method of treating or preventing a cerebral function disorder which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.
- 10 21. The method of claim 20 wherein the bupropion metabolite is optically pure.
22. The method of claim 21 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.
- 15 23. The method of claim 20 wherein the the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is adjunctively administered with a therapeutically or prophylactically effective amount of a second pharmacologically active compound.
- 20 24. The method of claim 20 wherein the cerebral function disorder is Parkinson's disease.
25. The method of claim 20 wherein the cerebral function disorder is epilepsy.
- 25 26. A method of eliciting smoking cessation which comprises administering to a patient who smokes tobacco a therapeutically effective amount of a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.
27. The method of claim 26 wherein the bupropion metabolite is optically pure.
- 30 28. The method of claim 27 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.

29. The method of claim 26 wherein the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is administered orally, mucosally, or transdermally.

5 30. The method of claim 29 wherein the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is administered transdermally.

10 31. The method of claim 26 wherein the bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is adjunctively administered with a therapeutically effective amount of nicotine.

15 32. The method of claim 31 wherein the nicotine and/or bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is administered orally, mucosally, or transdermally.

33. The method of claim 32 wherein the nicotine and/or bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof is administered transdermally.

20 34. A method of treating or preventing incontinence which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.

25 35. The method of claim 34 wherein the bupropion metabolite is optically pure.

36. The method of claim 35 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.

30 37. The method of claim 34 wherein incontinence is stress urinary incontinence.

38. The method of claim 34 wherein the patient is a human of an age greater than 50 years or less than 13 years.

39. A pharmaceutical composition which comprises a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.

5 40. The pharmaceutical composition of claim 39 wherein the bupropion metabolite is optically pure.

41. The pharmaceutical composition of claim 40 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.

10 42. The pharmaceutical composition of claim 40 wherein said pharmaceutical composition further comprises a second pharmacologically active compound selected from the group consisting of selective serotonin reuptake inhibitors, 5-HT₃ inhibitors, and nicotine.

15 43. A dosage form comprising a bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.

44. The dosage form of claim 43 wherein said dosage form is solid.

20 45. The dosage form of claim 43 wherein said dosage form is a sterile solution.

46. The dosage form of claim 43 wherein said dosage form is a transdermal patch.

25 47. The dosage form of claim 43 wherein the bupropion metabolite is optically pure.

48. The dosage form of claim 47 wherein the optically pure bupropion metabolite is optically pure (S,S)-hydroxybupropion.

30

49. The dosage form of claim 43 wherein said dosage form further comprises a second pharmacologically active compound selected from the group consisting of selective serotonin reuptake inhibitors, 5-HT₃ inhibitors, and nicotine.

5 50. The dosage form of claim 43 wherein said dosage form is suitable for oral, mucosal, or transdermal administration to a patient.

10 51. A dosage form suitable for transdermal administration to a patient which comprises nicotine and a bupropion metabolite or pharmaceutically acceptable salt, solvate, or clathrate thereof.

52. A lactose-free solid dosage form comprising an optically pure bupropion metabolite or a pharmaceutically acceptable salt, solvate, or clathrate thereof.

15 53. The dosage form of claim 52 wherein said dosage form is an oral dosage form.

20 54. A process for preparing optically pure (S,S)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol or a pharmaceutically acceptable salt, solvate or clathrate thereof which comprises:

asymmetrically hydroxylating Z-1-(3-chlorophenyl)-1-*tert*-butyldimethylsilyloxy-1-propene to form an intermediate;

reacting the intermediate with 2-amino-2-methyl-1-propanol to form (S,S)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol; and

25 isolating the (S,S)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol.

55. A process for preparing optically pure (R,R)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol or a pharmaceutically acceptable salt, solvate or clathrate thereof which comprises:

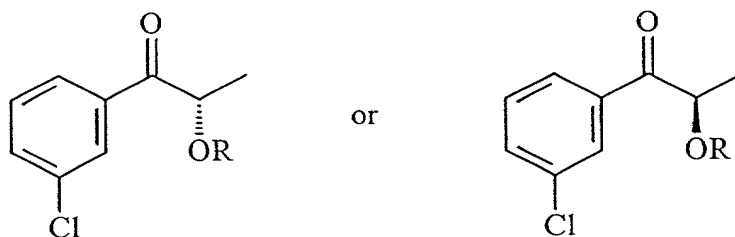
asymmetrically hydroxylating Z-1-(3-chlorophenyl)-1-*tert*-butyldimethylsilyloxy-1-propene to form an intermediate;

reacting the intermediate with 2-amino-2-methyl-1-propanol to form (R,R)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol; and

isolating the (R,R)-2-(3-chlorophenyl)-2-hydroxy-3,5,5-trimethyl-morpholinol.

56. The process of claim 54 or 55 wherein the intermediate formed by the asymmetric hydroxylation of Z-1-(3-chlorophenyl)-1-*tert*-butyldimethylsilyloxy-1-propene is an α -hydroxy ketone activated by trifluoromethane sulfonic anhydride.

57. A compound of the formula:



wherein R is selected from the group consisting of hydrogen, triflate, tosylate, and nosylate; or a pharmaceutically acceptable salt, solvate, or clathrate thereof.